The quest for optimal labour induction drug delivery

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Induction of labour, once considered a practice to be avoided unless absolutely necessary, is becoming increasingly common. Many different methods of induction of labour, ranging from mechanical to pharmacological, are available and when used in various combinations and sequences, offer an overwhelming number of possibilities. With misoprostol being one of the most common and efficacious labour induction agents, the quest to optimise the route and dosing of the drug are important. Misoprostol is included on the World Health Organization's list of essential medicines and can be administered by many routes and dosing regimens (World Health Organization *Who Tech Rep Ser* 2015;994:1–546; Elati et al. *BJOG* 2009;116:61–9). The optimal dosing and route of delivery remain undecided.

When a clearly superior drug strategy eludes providers, new technologies and products can be tempting as they seem to present a logical, optimal solution to drug dilemmas. Nevertheless, these new strategies or products must be tested. Wallströom et al. (*BJOG* 2019;126:1148-55) compare a slow-release misoprostol vaginal insert (MVI) with the WHO recommended dose of oral misoprostol in a randomised controlled trial. The authors did an excellent job of examining the many factors that determine a superior labour induction agent, including time to delivery, caesarean delivery rate, adverse maternal and neonatal outcomes, and patient satisfaction. The trial was well planned to have as low a risk of bias as possible. Typical to many labour induction studies involving different routes of drug, the authors did not blind the interventions by using a placebo for the alternative routes. The analytical methods, including censoring women who underwent a caesarean, were appropriate.

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~~Comparing oral misoprostol solution to the MVI, the authors found no difference in time from induction to vaginal delivery (median 23.2 versus 21.1 hours, *P* = 0.31), vaginal delivery within 24 hours (50.5% versus 55.7%, *P* = 0.16), or rate of caesarean delivery (31.9% versus 26.6%, *P* = 0.09).~~ Comparing oral misoprostol solution to the MVI, the authors found no difference in time from induction to delivery (median 23.2 versus 21.1 hours P = 0.31), vaginal delivery within 24 hours (50.5% versus 55.7%, P = 0.16), or rate of caesarean delivery (31.9% versus 26.6%, P = 0.09). MVI not only failed to show improvement over oral misoprostol solution in delivery outcomes, but also the MVI group was found to incur more adverse events. A higher proportion of women in the MVI group developed hyperstimulation necessitating tocolytics (4.0% for oral versus 22.7% for MVI, $P < 0.01$). Women in both groups had similarly high rates of satisfaction with their delivery experience ($P = 0.55$).

When two interventions may be clinically equivalent and satisfaction with the methods are also equivalent, the cost of each intervention can be weighed into the clinical decision-making. The authors presented the cost of each therapy in the Methods but did not discuss the implications in the Results or Discussion. Women in the oral misoprostol group received an average of 5.5 doses, which calculates to a mean total cost of 13.75 SEK. Each MVI costs 'about 1000 SEK'. Hence, the women receiving an MVI would incur more than 70 times the drug cost compared with those receiving oral administration. Given the lack of difference in efficacy and the potential increased adverse effects and cost with MVI, the authors reach the conclusion that oral misoprostol remains the first-line recommendation.

Although this study has its limitations, including being limited to nulliparous low-risk women, it was well executed. This trial highlights the need to rigorously test new medications and technologies, something the authors accomplished. Comparing the efficacy, safety and cost data, and synthesising trials systematically can lead us closer to an optimal strategy for labour induction (Alfirevic et al. *BJOG* 2016;123:1462–70).

Disclosure of interests

None declared. Completed disclosure of interest forms are available to view online as supporting information.